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VICE PRESIDENT
CHEMSTAR

November 16, 2005

201-16101

**American
Chemistry
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Stephen E. Johnson, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116
Attention: Chemical Right-to-Know Program

Re: Acetylene (CAS No. 74-86-2)

Dear Administrator Johnson:

The ACC Acetylene Panel¹ is pleased to respond to comments from the Environmental Protection Agency with respect to the Panel's submission of a dossier of robust summaries and test plan under the U.S. EPA High Production Volume Chemical Program.

Summary of EPA Comments

The Environmental Protection Agency has reviewed the acetylene robust summaries and test plan, and agrees that adequate data exist to characterize the substance's physicochemical properties and environmental fate for the purpose of this program. The EPA also finds that, because acetylene is a gas that forms highly explosive mixtures in air, the estimated data provided for ecological effects are acceptable.

EPA has noted that no claim was made that acetylene should be considered as a closed system intermediate, and thereby be considered a candidate for reduced testing. The Agency commented that the submitter needs to better explain that the data provided have adequately addressed all health effects endpoints or to supply additional test data.

With respect to health effects data, the Agency commented that adequate data have been provided for acute toxicity and gene mutation, but that the endpoints for developmental and reproductive toxicity and chromosomal aberrations have not been adequately addressed.

Response to Comments

The Acetylene Panel has considered EPA's recommendation to provide chromosome aberration data. The Panel agrees that such a study can be done with precaution, and therefore has agreed to modify the test plan to conduct such a study. This test will be done *in vitro*, using Chinese Hamster lung or ovary cells. The material will be tested at a maximum concentration of 50% of the LEL (about 11,500 ppm or 1.1% in air) to mitigate the potential for explosion. Concentrations of acetylene in the atmosphere will be measured, to confirm exposure. The Panel will use the purest form of acetylene commercially available.

¹ Member companies of the Acetylene Panel include Air Liquide America Company, BASF Corporation, Chevron Phillips Chemical Company LP, Dow, DuPont, Rohm and Haas, Lyondell Chemical Company, Shell Chemicals Ltd., Praxair, Inc.



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The Acetylene Panel believes that existing repeated dose studies are adequate for purposes of the HPV Program and does not believe that testing for developmental/reproductive toxicity is needed or practical, for reasons stated in the original submission. These (together with additional reasoning) are detailed below. The explanation is based on practical considerations (limited exposure and the explosive nature of acetylene) and existing toxicological data.

(a) Limited exposure:

The Agency is correct in stating that the submitter is not making a formal claim that acetylene meets the definition of a closed system intermediate. A recognized major use is in welding torches (which is not an industrial intermediate). The Panel does believe, however, that any workplace exposures to acetylene in welding applications are exceedingly low and for short duration, such that any exposures would be expected to be well below a level that is hazardous to health. Acetylene is and must be manufactured in a closed system, because any meaningful escape of this gas presents a serious explosion hazard. Similarly, use of acetylene as an industrial intermediate (which amounts to 80% of production) is carried out in enclosed systems for the same reason.

The most likely scenario for human exposure to acetylene is in its use for welding (amounting to 20% of production), especially in small welding shops where welding is not automated and/or does not include engineering controls. It is possible that at the start of a welding operation, when the welding torch is ignited, a very small amount of acetylene may escape without combustion in the split second when the valve to the acetylene tank is opened and before ignition. It is inconceivable, however, that the amount liberated in this extremely short interval would be sufficient to contribute significantly to an appreciable room concentration of acetylene. Once ignition takes place, the acetylene is completely consumed by combustion (the temperature of the welding torch is > 3300 degrees C). If that were not the case, a serious explosion hazard could develop through gradual concentration build-up. In fact, acetylene welding has been conducted daily without incident (except in very rare cases) in many locations for decades. This well established, *de facto* record of safety in acetylene welding supports the absence of acetylene air concentration buildup during welding operations.

(b) Toxicological and safety considerations:

Because the potential for exposure to acetylene is so limited, the intents of safety preclude any unnecessary testing that would require significant air concentrations of acetylene to be maintained for substantial periods of time. The animal studies proposed by the Agency on developmental and reproductive toxicity will involve maintaining inhalation chambers for prolonged periods with concentrations of acetylene at a significant fraction of the Lower Explosive Level. As shown below, data already exist that demonstrate that health effects from acetylene exposure occur only at doses several times higher than the LEL (Franklin and Miklos, 1933). Indeed, the overwhelming consequence of acute or repeated exposure to high levels of acetylene is narcosis. This effect was reversible and no adverse effects were seen at cellular level on major organs.

We acknowledge that the Franklin and Miklos studies were not conducted to current test standards and did not examine organs associated with reproduction or developmental parameters. Acetylene was, however, tested in several animal species for exposure periods of up to 90 days and it did not cause significant treatment-related adverse findings other than reduced survival.

There was no evidence of gross or histological damage to parenchymatous cells of the heart, lung, liver, kidney and spleen. In rat and guinea pig, the NOAEL was 800,000 ppm.

In addition to this work, repeated exposure data are available on the analog methylacetylene. Studies reported in rats and dogs (6h/day, 5 days/week for 6 months) indicate simple asphyxiant properties at a concentration of 28,700 ppm. There was no observed effect of treatment on any hematological, urinalysis or biochemical index of toxicity and the gross appearance of all organs and microscopic examinations of the lung, liver, kidney, heart, spleen and GI tract in exposed animals at study termination were normal.

Since the test plan and robust summary document were submitted, we have located a dichloroacetylene carcinogenicity study in which acetylene was used as a control (Carcinogenesis, 5: 1141 – 1420, 1984). In this study, mice and rats were exposed nose-only “to a maximum of 20 ppm acetylene” for 12 or 18 months. Since endpoints other than tumorigenicity were not measured in this study, this cannot be used to fill the repeated dose endpoint. Additionally, we do not consider this study a valid study to assess the carcinogenicity of acetylene, since an air-exposed control group was not included, the study did not appear to be conducted according to GLP, and actual concentrations of acetylene that the animals were exposed to were not determined. Since historical control data for nose-only, air-exposed NMRI mice and Wistar rats for the exposure times listed in the study (12 and 18 months) and all the tumor types measured were not available, we cannot determine if pathological findings in acetylene-exposed animals were actually due to acetylene exposure.

Path forward

Based on text already presented in the test plan and additional reasons stated above, repeated dose, reproductive and developmental toxicity testing will not be conducted. We do, however, recognize that a chromosome aberration study is to be provided and the Panel will conduct testing to address this data end point. When this study is completed, the Panel will revise the dossier and test plan to include the new robust summary and finalize the submission.

Sincerely yours,

Courtney M. Price
ice President, CHEMSTAR

201-10201

High Production Volume Challenge

Revised Test Plan

for

**Acetylene
CAS No. 74-86-2**

Prepared by:

**American Chemistry Council
Acetylene Panel**

November 16, 2005

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1.0 Introduction

The Acetylene Panel¹ (Panel) of the American Chemistry Council (ACC) has agreed to supply screening level hazard and use information under the U.S. EPA High Production Volume (HPV) Challenge Program for acetylene (CAS No. 74-86-2). This plan identifies existing data of adequate quality for this chemical, and how the data serve to address the HPV Challenge screening endpoints.

2.0 Designation of Test Substance

Test Substance

The test substance presented in this test plan is acetylene (CAS No. 74-86-2). Its molecular structure is as follows:



Acetylene is a well-known industrial gas. It is the lowest molecular weight analog of the class of neutral organic, acetylenic compounds. This substance is also known as ethyne.

Nearest Analog

The next higher homolog (nearest analog) of acetylene is methylacetylene (CAS No. 74-99-7), also known as propyne or 1-propyne. Its molecular structure is as follows:



Data for methylacetylene will be used to address the repeat dose and bacterial reverse mutation assay endpoints for acetylene in this test plan. Information for methylacetylene should be predictive of acetylene for the following reasons:

- Methylacetylene, as the next higher acetylenic homolog, is the most closely related chemical to acetylene in molecular structure and size, and has the identical functionality (the carbon-carbon triple bond);
- Methylacetylene, also a gas at ambient temperatures, exhibits physical/chemical properties that are similar to acetylene, as shown in Table 1; and
- The acute toxicity of methylacetylene in mammals is closely similar to that of acetylene.

The reasons for choosing methylacetylene are consistent with the EPA draft guidance for “The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program.” Based on a review of the data, it is concluded that methylacetylene is a valid analog for acetylene and that the uptake, metabolism, ecotoxicology and health effects of the two compounds is

¹ The current members of the Acetylene Panel are: Air Liquide America Company; BASF Corporation; Chevron Phillips Chemical Company; Dow; DuPont; Equistar Chemicals, LP; Praxair, Inc.; Rohm and Haas Company; and Shell Chemicals Limited.

expected to be very similar. Therefore, data comparison is used for those instances where valid and reliable data are available for methylacetylene but not for acetylene.

Manufacture of Acetylene

In the United States, six companies currently manufacture acetylene for use primarily as a chemical intermediate that is used in closed systems. U.S. manufacturing capacity in 2004 totaled 247 million pounds (Lacson *et al.*, 2004). This capacity included both captive and merchant capabilities, but did not include smaller amounts made by industrial gas producers for use in acetylene torches.

The major producers in the U.S. manufacture acetylene by either the partial oxidation of natural gas or as a co-product from the steam cracking of ethylene (Lacson *et al.*, 2004; Kirk-Othmer, 1995). Acetylene produced by either method is used primarily as a closed system industrial intermediate. Minor producers manufacture smaller amounts of acetylene by reacting calcium carbide with water manufactured using the carbide process. This acetylene is used primarily in acetylene torches.

Some commercial grades contain toxic impurities, such as phosphine, hydrogen sulfide, ammonia or arsine, depending on the production process. Phosphine, a minor impurity in acetylene primarily produced from calcium carbide, has a TLV-TWA of 0.3 ppm and a TLV-STEL of 1 ppm (ACGIH, 2001).

Uses of acetylene

In the year 2000, approximately 80% of U.S. production was used as a closed system industrial intermediate in the synthesis of other chemicals (Lacson *et al.*, 2001). The remaining 20% of production was predominantly used in oxyacetylene torches for welding and metal cutting (Lacson *et al.*, 2001). Currently, 96% of manufacturing capacity of the major manufacturers is slated for use as a closed system industrial intermediate. Most of this use occurs at the manufacturing sites, because of the economic and physical impracticality of transferring large quantities of acetylene gas to other sites. Some acetylene is also transferred through pipes to neighboring facilities for conversion to other products. Products made from acetylene include vinyl chloride monomer, acetylene black, vinyl fluoride, N-vinylcarbazole, N-vinylcaprolactam and other derivatives such as 1,4-butanediol, vinyl ethers, N-vinyl-2-pyrrolidone, and vinyl esters. Acetylene was used in the early 1900's as an anesthetic (under the name Narcylene). It is no longer used as an anesthetic because better, less explosive alternatives are available. No uses of acetylene in consumer products are known. Since the majority of acetylene is used as a closed system industrial intermediate and as a fuel for oxyacetylene torches, minimal occupational exposure, with no consumer exposure, is expected.

3.0 Criteria for Determining Adequacy of Data

All identified available studies were reviewed and assessed for adequacy according to the standards of Klimisch *et al.* (1997). Studies receiving a Klimisch rating of 1 or 2 are considered to be adequate.

4.0 Available Data

The summary of available data for acetylene (as shown in Table 5) was constructed after a careful evaluation of all identified existing data (see below).

4.1 Chemical and Physical Properties

Key chemical/physical properties of acetylene and methylacetylene are discussed in the following sections and summarized in Table 1.

4.1.1 Melting Point

A melting point of -80.8°C for acetylene is reported by Lide (1992-1993). The same reference cites a melting point of -101.5°C for methylacetylene.

4.1.2 Boiling Point

A boiling point of -84°C is reported for acetylene by Lide (1992-1993). The same reference cites a melting point of -23.2°C for methylacetylene.

4.1.3 Vapor Pressure

A vapor pressure of 6,969.2 hPa is reported for acetylene by Daubert and Danner (1989). This value was calculated from experimentally derived coefficients. The vapor pressure of methylacetylene is 5,155 hPa (Clayton and Clayton, 1981-2).

4.1.4 Octanol/Water Partition Coefficient

The method of Hansch and Leo (1995) was used to estimate a log Kow of 0.37. The same method was used to estimate a log Kow of 0.94 for methylacetylene.

4.1.5 Water Solubility

A measured water solubility of 1,230 mg/l at 1,010 hPa and 20°C is cited in Grayson (1978). This value is consistent with the water solubility value of 1,200 mg/l reported in the Hazardous Substances Data Bank (2003). These values indicate that acetylene theoretically has appreciable water solubility. However, the likelihood that acetylene concentrations in water would ever approach this level (except under controlled or forced conditions) is remote based on its very strong tendency to volatilize to its normal gaseous state (See Table 2 and Section 4.2.3). The water solubility of methylacetylene is reported to be 3,640 mg/l (McAuliffe, 1966).

4.1.6 Explosivity

Acetylene is a gas that forms highly explosive mixtures in air across a broad range of concentrations. The lower explosive limit (LEL) is 2.5% (25,000 ppm) in air (National Fire Protection Association, 1997).

4.1.7 Summary/Test Plan for Physical Properties

Acetylene has been a commercial industrial chemical for many decades, and its key physical properties are well established. Although the data were determined long ago (and therefore not generated using current guideline methods), the data should be accepted as reliable. Measured data are available for many of the required physical property endpoints. The melting and boiling points

are -80.8°C and -84°C, respectively. The calculated vapor pressure is 6,969.2 hPa at 25°C. The estimated octanol/water partition coefficient is 0.37. Based on its very high vapor pressure, both the estimated partition coefficient and the appreciable water solubility of 1,200 mg/l are largely of only theoretical relevance. No new testing for physical properties is proposed.

Table 1 shows the comparison of physical properties for acetylene and the nearest analog, methylacetylene. The similarities of these properties are noted.

Table 1. Chemical/physical Properties of Acetylene and Methylacetylene

<i>Endpoint</i>	<i>Acetylene</i>	<i>Methylacetylene</i>
Molecular weight (grams/mol)	26.04	40.07
Melting point	-80.8°C ^a	-101.5°C ^a
Boiling point (at 1016 hPa)	-84 °C ^a	-23.2°C ^a
Relative density (at -82°C)	0.6208 ^a	0.7062 ^a
Vapor pressure (hPa)	6,969.2 ^b (at 25° C)	5,155 ^a (at 20° C)
Partition coefficient (Log Pow or Kow)	0.37 ^b	0.94 ^b
Water solubility (mg/l at 25 ° C)	1,230 ^a	3,640 ^a

^a Measured value; ^b Estimated value

4.2 Environmental Fate/Pathways

The results of environmental fate modeling and studies are discussed below and summarized in Table 2.

4.2.1 Photodegradation

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/Aop (v1.90). An overall hydroxyl radical rate constant of 8.15 E-13 cm³/(molecule*sec) was calculated based on the summation of individual rate constants for each bond fragment in the molecule using the program algorithm. A half-life of 13.1 days was calculated assuming a constant concentration of OH radical and pseudo first order kinetics. Since acetylene is a gas (except at temperatures well below 0°C), atmospheric photodegradation is expected to be the most significant route of degradation in the environment.

4.2.2 Stability in Water

Because the material is a gas, rapid volatilization is by far the relevant environmental fate pathway for acetylene in the hydrosphere. Therefore, it is not necessary to conduct experiments to determine water stability. Since acetylene does not contain functional groups that are known to be readily hydrolyzed (i.e., ester groups, nitriles, amides, etc.), it is not expected to hydrolyze readily under neutral ambient conditions. The carbon-carbon triple bond is generally recognized to be stable in water. Therefore, the small amount of material that may be present in the hydrosphere is expected to remain intact until it evaporates.

4.2.3 Fugacity

Level III fugacity modeling has been conducted on acetylene using the EPIWIN model. Inputs to the program were CAS No. 74-86-2, a melting point of -80.8 °C, a boiling point of -84°C, a vapor pressure of 6,969.2 hPa and water solubility of 1,200 mg/l. The emission rate inputted into the program for air was 1,000 kg/hr (model default value). The emission rates inputted to water, soil and sediment were 0 kg/hour. These emission rates are more in keeping with manufacturing and use processes that are extremely unlikely to emit significant emissions to these media, and forcing acetylene into these media would be very difficult based on the physical properties of acetylene. Model default emissions of 1,000 kg/hr (87,600,000 kg/year) to the air are beyond reasonable worst-case assumptions, especially from point sources. The following half-lives were calculated: $T_{1/2}$ air = 298 hrs, water = 360 hrs, soil = 360 hrs, and sediment = 1,440 hrs. A Henry's Law Constant of 0.024 atm-m³/mol and a soil sediment partition constant (K_{oc}) of 14.3 were estimated using the EPIWIN/Henry and PCKOC Programs, respectively. The percent mass balances predicted for acetylene in air, water, soil and sediment are shown in Table 3. The results show that 99.9% of acetylene will remain in the atmosphere after being discharged into it.

4.2.4 Biodegradation

Since acetylene is a gas and 99.9% partitions to the air according to the Fugacity Level III model, biodegradation is not an important route for removal of the material from the environment. Furthermore, since standard OECD biodegradation tests are not designed to assess the relative biodegradability of gaseous materials, such tests will be difficult to perform and will not adequately assess the ability of the material to biodegrade in the environment. Since the material is a gas, the primary means of degradation of the vast majority of the material in the environment is photodegradation, which supports the conclusion that biodegradation is irrelevant.

4.2.5 Summary/Test Plan for Environmental Fate Parameters

Estimated values are available for the hydroxyl radical induced photolysis rate constant and atmospheric half-life, Henry's Law Constant and Fugacity Level III environmental transport parameters. These values indicate that acetylene has a very strong tendency to partition to the atmosphere, where it undergoes photodegradation. Standard biodegradation tests have not been performed with acetylene and are not considered relevant studies to conduct on a gas that will mainly partition to air. Although the material is expected to be stable in water, any material present in water will rapidly evaporate. Therefore, no testing for water stability (hydrolysis) is proposed.

Table 2. Environmental Fate Parameters for Acetylene

<i>Endpoint</i>	<i>Value</i>
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant) ^a (Atmospheric $T_{1/2}$) ^a	8.15 E-13 cm ³ /molecule-sec 13.1 days
Stability in Water	Should not hydrolyze
Henry's Law Constant ^a	0.024 atm-m ³ /mol
Environmental transport (Fugacity Level III mass percentages) ^a	Air = 99.9 Water = 0.104 Soil = 0.0101 Sediment = 0.000177
Biodegradation	Not applicable

^a Estimated using EPIWIN

4.3 Aquatic Ecotoxicity

Since acetylene is a gas that will partition to air and rapidly evaporate from the aqueous environment, ecotoxicity testing is not considered relevant. Nonetheless, some toxicity tests have been conducted in several aquatic species. The results of this testing (along with ECOSAR modeling) are discussed below and summarized in Table 3.

Table 3. Ecotoxicity of Acetylene

<i>Species</i>	<i>LC50/EC50 (mg/l) (time)</i>
Fish (unspecified)	approx. 500 ^a (96 hour)
Lepomis sp.	> 1,000 (1 hour) ^b
Minnow (unspecified)	> 17 (1 hour) ^b
Trout fingerlings	200 (33 hour) (limit of toxicity) ^b
Cyprinus auratus (goldfish)	400 (24-48 hour) (limit of toxicity) ^b
Fingerling chinook salmon	3,500 (72 hours) (limit of toxicity)
Young rainbow trout	3,000 – 5,000 (72 hours) (limit of toxicity)
Daphnia magna	approx. 480 ^a (48 hour)
Green algae	approx. 275 ^a (96 hour)

^a Estimated using EPIWIN; ^b Given a reliability rating of 4 due to lack of information

Since experimental conditions were not listed and the primary references were not available for the fish toxicity studies, it is not known whether the concentrations listed are nominal or measured, or if the studies were conducted using flow through or static methods. If the experiments were performed using closed systems that would force acetylene into the water and minimize volatilization, the relevance of the results for the aquatic environment would be questionable. Such attempts would eliminate airspace around the liquid and lead to deoxygenation. In conclusion, the testing and modeling that have been done are adequate for HPV purposes. No additional testing is proposed.

4.3.1 Acute Toxicity to Fish

The 96-hr LC50 value for fish estimated by EPA's ECOSAR model for the neutral organic class is approximately 500 mg/l. This is similar to concentrations reported as causing death to an unknown number of trout fingerlings and goldfish in the OHM/TADS database, and less than concentrations reported to cause toxicity in fingerling chinook salmon and young rainbow trout. The concentrations reported for salmon and rainbow trout (3,500 and 3,000-5,000 mg/l respectively) are suspect, since, these values exceed the measured water solubility of acetylene. Since references for these studies were not given in the database and were not available, they could not be reviewed. Therefore, reliability ratings of 4 (not assignable) were designated for these studies.

4.3.2 Acute Toxicity to Aquatic Invertebrates

EPA's ECOSAR model for the neutral organic class predicts a 48-hour EC50 value of approximately 480 mg/l for *Daphnia*. No experimental test data were available.

4.3.3 Acute Toxicity to Aquatic Plants

The 96-hr EC50 value calculated for green algae by the ECOSAR model for the neutral organic class is approximately 275 mg/l. No experimental test data were available.

4.3.4 Summary/Test Plan for Ecotoxicity

The available ecotoxicity data, combined with the ECOSAR results, adequately address the ecotoxicity endpoints for HPV purposes. Since the material is a gas, it will evaporate quickly from water. Tests that are performed in closed systems in the laboratory will not adequately simulate environmental conditions in which acetylene will remain in the atmosphere. Experimental studies performed to prevent volatilization may also be accompanied by deoxygenation, which is not expected to actually occur in environmental bodies of water. In the aqueous environment, acetylene should not be present at concentrations estimated by ECOSAR to cause toxicity to aquatic species. No additional ecotoxicity testing is proposed.

4.4 Human Health Data

Because acetylene is a gas, it is not relevant to test the material using oral or dermal routes of application. Inhalation is the only significant potential route of exposure.

4.4.1 Acute Mammalian Toxicity

With decades of production and use, the acute toxicity of acetylene is well understood to be that of a simple asphyxiant. Data regarding the acute inhalation toxicity to animals and humans clearly show that acetylene is of a very low acute toxicity. Overall, the data support a rat LC50 > 100,000 ppm.

In humans, acetylene is not acutely toxic below its lower explosive limit of 2.5% (25,000 ppm). Inhalation of 10% acetylene (100,000 ppm) for 1 hour does not cause acute toxicity. Inhalation of 33% or 35% has caused unconsciousness within 7 and 5 minutes, respectively (Davidson, 1925). Two deaths and a near fatality occurred after inhalation of 40% acetylene during manufacture with calcium carbide (Carreón, 2000; Jones, 1960). The cause of these deaths was attributed to the phosphate and arsine impurities in crude acetylene and carbon monoxide present in the work area.

In rats, a concentration of 78% acetylene (780,000 ppm) produced anesthesia in 15 minutes, and inhalation of 90% for 2 hours caused respiratory failure (Riggs, 1925). Inhalation of 850,000 ppm caused increased respiratory volume and frequency and induced anesthesia in dogs, with rapid recovery (Heymans and Bouckaert, 1925). Therefore, the LC50 value in this study was greater than 850,000 ppm.

4.4.2 Repeated Dose Mammalian Toxicity

In 1933, Franken and Miklos looked for possible organ damage from the administration of acetylene at anesthetic concentrations to rats, mice, guinea pigs, rabbits, and dogs. Animals were exposed to acetylene in oxygen according to the scheme presented in Table 4.

Table 4. Test Conditions and Results for Franklin and Miklos Study (1933)

<i>Animal</i>	<i>Number Tested</i>	<i>Conc. (%)</i>	<i>Daily Exposure Time (hours)</i>	<i>Number Of Days Exposed</i>	<i>Total Exposure Time (hours)</i>	<i>Deaths</i>
Rat	16	25	1	7-93	7-93	6
Rat	10	50	2	1-8	2-16	9
Guinea Pig	7	50	2	1-9	2-18	7
Mouse	5	50	2	1-6	2-12	5
Rat	47	80	½	2-36	1-18	36
Rat	8	80	1	14	14	0
Guinea Pig	6	80	1	10	10	0
Rabbit	4	80	1	6-10	6-10	3
Dog	2	80	1	12	12	1

At the lower concentrations (concentrations were not stated) the animals appeared only slightly sleepy. At higher concentrations the majority of animals fell asleep after 15-20 minutes. In general, these animals were not in deep narcosis. The rats, rabbits, guinea pigs and dogs generally recovered from narcosis in a short time. However, the mice did not survive treatment. Some of the animals died spontaneously. Pneumonia was observed in most of these cases. Since pneumonia also was observed in control animals exposed only to air, it does not appear to be related to treatment. In treated animals that survived to termination, the authors found no evidence of cellular injury to the parenchymatous cells of the heart, lungs, liver, kidneys, or spleen. In rat and guinea pig, the 14 and 10 day (1 hr exposure/day) NOAELs were 80% (800,000 ppm). The fact that higher death rates were reported in rats exposed 1 hr/day to 25% (250,000 ppm) is likely due to the fact that the deaths were reported over a period of 7-93 days, rather than weekly or biweekly intervals.

Capillary hyperemia of the liver, kidneys and spleen was observed in some rats exposed to 25%. This effect was observed until at least the second day after the last exposure to the gas but was not evident in animals killed later (up to 5 days after the last exposure). Since capillary hyperemia was not observed in rats exposed to higher concentrations of acetylene, it does not appear to be test-material related. In conclusion, since repeated exposure of rats to a concentration (25%) that greatly exceeds any concentration that would be expected to occur in routine human working conditions did not cause any organ toxicity, it is expected that repeated exposure of humans to concentrations routinely encountered in the workplace would not cause organ toxicity.

The repeated dose toxicity of the analog methylacetylene has been studied in rats and dogs (Horn *et al.*, 1957). In this study, the animals were exposed to 28,700 ppm methylacetylene 6 hr/day, 5 days/week for 6 months. Rats and dogs reached an early plane of anesthesia (within 30 minutes) and generally recovered rapidly after each exposure. Forty percent of the rats and none of the dogs died over the course of the study. Gross pathology of the rats that died was limited to the lungs, which appeared dark red and remained distended when the thorax was opened. In exposed rats that survived to termination, the lungs also were discolored and remained distended. Microscopic pathology of the lungs showed definite pulmonary irritation. The remaining organs appeared to be within normal limits. There was no effect of treatment on any hematological, urine or biochemical index of toxicity in the dogs. The gross appearance of all organs examined and microscopic examinations of the lung, liver, kidney, heart, spleen and GI tract in exposed dogs were normal.

Overall, the authors of the study concluded that methylacetylene is of low repeated dose toxicity and the site of toxicity was limited to the lungs, even at extremely high concentrations (28,700 ppm).

4.4.3 Genetic Toxicity

4.4.3.1 Mutagenicity

In an Ames test employing three strains of *S. typhimurium* (TA97, TA98, TA100), acetylene did not induce mutations in both the absence and presence of metabolic activation (Hughes *et al.*, 1984). This test was given a reliability rating of 2 (valid with restrictions), since current guidelines recommend testing in 4 different *S. typhimurium* strains and a strain of *E. coli*.

In a more recent test conducted in *S. typhimurium* TA98, TA100, TA1535 and TA1537 and *E. coli* WP2uvrA, the related material methylacetylene did not cause an increase in mutations in any strain of Salmonella at any concentration in the absence or presence of metabolic activation (Araki *et al.*, 1994). However, there was a dose dependent increase in the number of mutations in *E. coli* WP2 uvrA in the absence or presence of metabolic activation.

Overall, the weight-of-evidence on acetylene and its surrogate (methylacetylene) indicate that acetylene is not mutagenic.

4.4.3.2 Chromosomal Aberration

No chromosome aberration tests were identified for acetylene or methylacetylene. An OECD Test Guideline 473 Study will be performed to fill this end point.

4.4.4 Reproductive and Developmental Toxicity

No adequate reproductive or developmental toxicity studies have been located for acetylene. It is not deemed appropriate or relevant to conduct new testing for these endpoints for these reasons (which are discussed in greater detail below):

- The American Conference of Governmental Industrial Hygienists (ACIGH) Threshold Limit Value (TLV) Committee did not consider acetylene to be of reproductive concern when establishing a TLV, which is based on acetylene being a simple asphyxiant;
- As acetylene is used primarily as a closed system industrial intermediate, or as a welding gas where it is combusted, there is only a remote likelihood that human beings can be exposed to meaningful concentrations of acetylene, even in the workplace;
- It has been demonstrated that acetylene is minimally toxic to mammals, except at exceedingly high doses. The repeated dose study on the acetylene surrogate methylacetylene indicated effects only at the site of administration (lungs), and no effects at other organs. Evidence indicates that mammals do not metabolize acetylene but instead eliminate acetylene rapidly and unchanged from the lungs. Reproductive and developmental effects are not likely to occur as they would be effects that are remote to the lungs;
- Acetylene has been used for over 100 years as an anesthetic and industrial chemical and during this time period no link between any reproductive or developmental effect and the use of acetylene has been established; and

- A high fire and explosion hazard would be associated with any testing at meaningful concentrations.

These reasons are discussed in further detail below.

4.4.5 Other Health Information

ACGIH Classifies Acetylene as a Simple Asphyxiant

The ACGIH has reviewed the toxicology of acetylene and found no reason to assign a TLV for the workplace, giving acetylene a simple designation as an asphyxiant (ACGIH, 2003). However, in order to stay within the TLV-TWA for the potential contaminant phosphine, the ACGIH recommends that the TWA for acetylene should not exceed 3,160 ppm (ACGIH, 1991). The recommended Exposure Limit Ceiling Value is 2,500 ppm (NIOSH, 1997).

Inability to Expose Workers or General Population to Meaningful Concentrations of Acetylene

Approximately 80% of acetylene produced is used as a closed system industrial intermediate to manufacture other chemicals. Much of this use is at the same site as manufacture, with the acetylene being transferred from the closed manufacturing and storage units to the conversion units via pipes. The other primary use (approximately 20% of production) is in oxyacetylene torches for welding and metal cutting where mixtures of acetylene/air or acetylene/oxygen mixtures are burned to provide a very high temperature heat source. In this operation, acetylene gas is released from closed cylinders through a nozzle jet that is ignited to form the hot flame. There is a split second interval between the opening of the valve to the acetylene cylinder and the point at which the acetylene/oxygen mixture is ignited. This short interval should not permit a sufficient quantity of acetylene to escape into the work area to provide a significant concentration in the worker breathing zone. If ignition does not take place shortly after the cylinder valve is opened, it must be shut again quickly for safety reasons. In welding, acetylene undergoes complete combustion (the temperature of the welding torch is > 3300 degrees C). If complete combustion did not occur, a serious explosion hazard could develop through gradual concentration build-up. In fact, acetylene welding has been conducted daily without incident (except in very rare cases) in many locations for decades. This well established *de facto* record of safety in acetylene welding documents the absence of acetylene air concentration buildup during welding operations.

Acetylene is contained in enclosed equipment during manufacture, storage, transport and use. While it is possible that acetylene gas could escape from gas cylinders, enclosed reactors, pipes and storage tanks, such escape would be a result of a non-routine, emergency circumstance, such as a line rupture or failed valve. In such cases, immediate action is required to prevent escape of significant quantities, since just 2.5% or greater concentrations in air form explosive and combustible mixtures that are given the highest flammability hazard ratings. Therefore, air concentrations must be held to much lower levels, and work areas must be evacuated if significant air concentrations start to develop via accidental release. In summary, the most meaningful hazard associated with acetylene is fire and explosion that would be life-threatening before toxicological hazards could develop.

Simple diffusion model calculations show maximum expected 1-hour average ambient concentrations at approximately 5.5 ppm, and at approximately 3 ppm for 24-hour values of

acetylene near a plant boundary. Urban concentrations of approximately 80 ppb and rural values of 1 ppb have been measured. Based on the "low toxicity and expected low ambient concentrations, acetylene does not pose a health or environmental hazard as an air pollutant" (Patterson *et al.*, 1976).

Demonstrated Minimal Toxicity

Acetylene is not acutely toxic below its lower explosive limit of 2.5% (25,000 ppm). It has been well established that acetylene behaves in mammalian systems primarily as a central nervous depressant and asphyxiant at high dose levels (100,000 ppm in air or above). It produces varying degrees of temporary and reversible narcosis when administered with oxygen in concentrations of $\geq 100,000$ ppm (10% in air). Repeated exposure of rats, mice, guinea pigs rabbits and dogs to concentrations $\leq 800,000$ ppm showed no evidence of cellular injury to the parenchymatous cells of the heart, lungs, liver, kidneys, or spleen (Franklin and Miklos, 1933). The only histologic findings in rats exposed an anesthetic concentration (28,700 ppm) of the related material methylacetylene for 90 days were confined to the lungs (Horn *et al.*, 1957).

While the repeated dose studies with methylacetylene did not show a NOAEL per se, the effects that were observed in dogs after 6 months of exposure to 28,700 ppm occurred within 30 minutes of exposure termination and are similar to those observed after acute exposure to organic materials that act as simple asphyxiants. The animals recovered quickly, and there was no observed effect of treatment on any hematological, urinalysis or biochemical index of toxicity. The gross appearance of all organs and microscopic examinations of the lung, liver, kidney, heart, spleen and GI tract in exposed animals at study termination were normal. Therefore, the NOAEL for effects other than acute effects was 28,700 ppm.

Limited data reported in the literature indicate that acetylene is rapidly absorbed and eliminated unchanged in the body (Adriani, 1952, 1962). The blood-gas partition coefficient of acetylene at normal hematocrit and body temperature is 0.833 (Jibelian *et al.*, 1981), indicating that the material has a greater propensity to be removed from blood than to be retained in it. Schrikker *et al.* (1989) have shown that, in man at rest, the rates of alveolar and mixed venous washout for acetylene calculated from the slopes of the of the alveolar plateau are 2.6% and 4.8% per second, respectively. Within 10 minutes of inhalation of acetylene for 15 minutes, the end tidal concentration was 8.0 % of its initial value. Together, these data support the contention that the lungs rapidly excrete acetylene. The gas also diffuses rapidly from the peritoneal and pleural cavities and diffuses through the skin. Therefore, acetylene is unlikely to persist in the body, even after repeated exposure to low concentrations that may be encountered in the workplace.

Long History of Use

Acetylene has been used for over 100 years as an anesthetic and industrial chemical, and few complications of using this gas have surfaced. According to the Hazardtext database, "there is no scientific evidence that repeated exposure to tolerable levels of acetylene leads to deleterious health effects." Epidemiological studies that have been published have failed to establish a link between use of acetylene and cancer. Exposure to acetylene is not associated with liver angiosarcoma in workers exposed to a number of materials (Waxweiler, 1981). Acetylene exposure also was not a risk factor in mortality from lung cancer in a case-referent study in which exposure to chemicals in an acetylene and phthalic anhydride plant accounted for one third of the total number of lung cancer deaths (Riboli *et al.*, 1988). In a pilot study conducted on 454 men, no associations were found between occupational exposure to acetylene and development of cancer (Siemiatycki *et al.*, 1982).

In a study conducted on 370 workers involved in acetylene cylinder manufacture between 1935 - 1975, an excess of deaths from lung cancer, and cancer of the stomach and pancreas was observed. However, an association between exposure to acetylene and lung cancer was not identified (Newhouse *et al.*, 1988). Acetylene also was not listed as a risk factor for developing cancer in a study involving 632 Danish male molders (Hansen, 1991). In two case-controlled studies, acetylene exposure was not identified as a risk factor for developing multiple myeloma (Morris *et al.*, 1986; Williams *et al.*, 1989). In a Texas plant, which utilizes acetylene and other chemicals to produce acrylate and methacrylate ester, the excess of total cancer deaths in those hired from 1958 to 1962 could not be correlated with job-related causes (Rohm and Haas, 1980).

In an epidemiological study conducted in Russia, the health status of an unknown number of pregnant women chemists who produced acetylene-vinyl acetate from 1972-1975 was compared to that of 84 pregnant women that did not work with chemicals (Talakina *et al.*, 1977). Twenty percent of the chemists were "sick", compared to 8% of the controls ($p < 0.001$). The nature of the illnesses was not mentioned; however, they were listed as being associated with temporary disability to work related to pathology of the pregnancy. No chemicals were identified in the study other than acetylene-vinyl acetate. Other materials that the female workers may have been exposed to were not mentioned or quantified. Additional variables that could have affected the results (e.g., age, number of years on the job, smoking, nutritional or social status) were not examined. Since the workers presumably were also exposed to vinyl acetate as well as acetylene, no causative relationship between exposure to acetylene and reproductive toxicity can be identified from this study. Due to the aforementioned limitations, this study cannot be considered valid. No other studies linking exposure of acetylene to any kind of reproductive concerns have been published over a long history of use.

Further Testing Would Be Hazardous

If further studies on acetylene were undertaken, they would provide little additional useful knowledge of the hazards of this substance without leading to study conditions (very high air concentrations) that would present a serious explosion hazard to animals and people. Reproductive and developmental testing would require inhalation chambers that contained greater than the lower explosive limit concentration (25,000 ppm) of acetylene in order to demonstrate a toxicological effect. These concentrations would have to be maintained for several hours per day (and confirmed by analytical monitoring) for 40-53 days (14 days prior to mating to postnatal day 5). Even if these conditions were achievable without incident, the data presented above indicate that the only manifestation of toxicity that would be observed is narcosis, asphyxiation of test animals, and pulmonary irritation.

4.4.6 Summary/Test Plan for Mammalian Toxicity

Acute and repeated dose studies that have been performed with acetylene in humans and animals and the repeated dose study with a related material (methylacetylene) adequately fill the acute and repeated dose endpoints. The bacterial mutagenicity tests that have been performed with acetylene and methylacetylene adequately characterize the potential for acetylene to cause mutagenicity. An OECD Test Guideline 473 Test will be conducted to fill the chromosome aberration endpoint. It is not considered necessary to perform reproductive/developmental toxicity tests in animals to characterize these endpoints since such toxicity has not surfaced after over a century of use of the material, acetylene is minimally toxic to mammals (except at exceedingly high doses or concentrations which are not likely to be present in the workplace), acetylene is rapidly excreted

from the lungs without metabolism, and performance of such studies would be extremely hazardous. Since the predominant use is as a closed system intermediate with little potential for exposure and the other use is as a fuel for oxyacetylene welding where the acetylene is consumed, potential exposure is severely limited.

5.0 Summary

Table 5 at the end of this section provides a summary of the available data for acetylene.

Physical Properties

Measured data are available for all required physical property endpoints except vapor pressure and partition coefficient. Acetylene has been a commercial industrial chemical for many decades and was well studied long ago with respect to its physical properties. Although the measured data were not determined by current guideline methods and testing predated good laboratory practices, the data should be accepted as reliable. The EPIWIN Kowwin-generated value for partition coefficient and the calculated value for vapor pressure is also considered reliable and accurate. No new testing is proposed.

Environmental Fate Properties

Estimated values are available for the hydroxyl radical induced photolysis rate constant and atmospheric half-life, Henry's Law Constant, soil sediment partition coefficient, and Fugacity Level III environmental transport parameters. These values indicate that acetylene has a very strong tendency to partition to the atmosphere, where it undergoes photodegradation. The small amounts of material present in the hydrosphere can be oxidized and reduced by sediment bacteria and are estimated by EPIWIN Biowin to be readily biodegradable. Although a measured hydrolysis rate constant is not available for acetylene, the material is soluble and theoretically stable in water, and any material present in water will rapidly evaporate. Therefore, water stability testing is not proposed.

Aquatic Toxicity

Since the material is a gas, it is not expected to be present in environmental waters at any of the concentrations shown to be toxic to fish or estimated by EPIWIN to be toxic to aquatic species. The utility of tests that have been performed is questionable since experimental details were not available. The hazard in conducting additional tests is not worth the risk, especially since guideline tests will not adequately simulate environmental conditions in which acetylene will remain in the atmosphere. No additional testing is proposed.

Mammalian Toxicity

Acute and repeated dose studies and bacterial mutagenicity tests that have been performed with acetylene and the related material methylacetylene adequately fill these endpoints. Therefore, no new testing of these three endpoints is proposed. An OECD Test Guideline 473 Test will be conducted to fill the chromosome aberration endpoint. No reproductive or developmental toxicity testing is proposed, due to the history, nature and uses of the material.

Table 5. Summary of Data Availability for Acetylene (CAS No. 74-86-2)

<i>Endpoint</i>	<i>Availability of Data</i>	<i>Proposed Testing</i>
Melting Point	A	None
Boiling Point	A	None
Vapor Pressure	A	None
Partition Coefficient	A	None
Water Solubility	A	None
Photodegradation	A	None
Stability in Water	NA	None
Biodegradation	NA	None
Transport between Environmental Compartments (Fugacity)	A	None
Acute Toxicity to Fish	A	None
Acute Toxicity to Aquatic Invertebrates	A	None
Acute Toxicity to Aquatic Plants	A	None
Acute Toxicity	A	None
Repeated Dose Toxicity	R	None
Genetic Toxicity-Mutagenicity	R	None
Genetic Toxicity-Chromosomal Aberration	N	OECD 473
Reproductive Toxicity	N	NP
Developmental Toxicity	N	NP

A = Adequate data exists.

N = No data were available

R = Read across.

NA = Information is presented which highlights the lack of relevance of data for the endpoint and is therefore, not applicable.

NP = Not proposed. See Sections 4.4.4 and 4.4.5

6.0 References

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